

The Life of a Neuron: Parkinson's and the Dopaminergic Neuron

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Being a neuron is a tough job. The hours are long, the pay is nonexistent, and the workplace is cramped. Even so, this job is everything to me. I used to be just another busy, dopaminergic neuron in the substantia nigra of the brain, totally in charge of motor movement through the dopamine neurotransmitter. All of us neurons worked hard to facilitate movement, from his first steps to the time he learned to ride a bike and even when he danced with his wife on their wedding day. Those days seem long ago as I look around me today. Most of my friends have died and our decreased numbers have left our human with hand and leg tremors that limit his mobility. I feel that I may soon die too and as the workforce diminishes, his symptoms will only worsen. While this might seem like a depressing end for a neuron, things weren't always so bad. Allow me to take you back to the very beginning when I was just a stem cell. I was an undifferentiated cell of an organism that could have given rise to indefinitely more cells of the same type, on the verge of discovering my role in life.

For all of us neurons, our story begins during a spectacular time in embryonic development called neurogenesis. Before we ultimately became neurons, we were stem cells. As the baby developed, we turned into precursor cells for neurons. We eventually turned into neuroblasts, entering the rookie stage for neurons. With the help of the radial glial cells, we were shown the part of the brain we would reside in for the rest of our lives and were given a highway to follow. This was the moment I discovered that I was meant to be a dopaminergic neuron. A young neuron, I moved eagerly to my new workplace: the substantia nigra.

"Hello everyone!", I called out as I finally made my way to the substantia nigra. I was greeted with a warm response and I got to work, preparing for my functions which would come to include not only voluntary movement, but an array of other behavioral processes such as mood, reward, and stress. The presence of dopamine defined this area of the brain because our division in the substantia nigra is the main source of dopamine in the central nervous system. As Joseph, the human we inhabited, matured, he advanced from small and simple motor movements, such as opening and closing his newborn hands, to much more complex ones, such as running and climbing. When his activities became more rigorous, I became busier. Things went smoothly for 55 years but after Joey celebrated his birthday with his family in October of 2011, I began to learn of a sinister disease attacking his brain.

Just like many neurological diseases, the first signs are insignificant and anecdotal. I recall a conversation I had with one of my late neuron colleagues a couple of months after Joey's 55th birthday, the beginning of the Parkinson's disease.

"Hey, did you hear what happened over at the olfactory bulb recently?", he began, a concerned note in his voice. The olfactory bulb is on the inferior side of the human brain and in charge of smell.

"No, I haven't", I replied, as other neurons began to listen in on our conversation.

"Apparently, there have been reports of alpha-synuclein clumps in the olfactory bulb and they're causing problems with Joey," my colleague told me.

Joey wasn't exactly the young, athletic man he used to be, and his metabolism had slowed down, so at that point I wasn't too concerned by this news.

"So, he's losing his sense of smell then?", I inferred, trying to sound calm and logical.

"Yeah, he's noticed he can no longer identify things by smell, even those that he has experienced before," my neuron colleague finished. Loss of smell was a strange symptom to have as otherwise, Joey felt fine. I thought that maybe this was a temporary condition and that perhaps it would go away just as suddenly as it had appeared. However, tremors in his hands soon followed.

When other dopaminergic neurons began to die around me, I knew that something was going wrong in Joey's brain. This process,

called neurodegeneration, left a deficiency of dopamine in the brain because the neurons that were dying were vital in producing this neurotransmitter in the substantia nigra. The actual process that was causing cells like me to die was not clear and when Joey received the diagnosis from his physician, all the remaining neurons in the substantia nigra learned that there was no cure for his Parkinson's. The treatment that they offered was in the form a drug called Levodopa, an amino acid that could cross the blood brain barrier and increase the dopamine concentration in the brain, helping me and the other dopaminergic cells with the workload after we had lost a significant amount of our workforce. L-DOPA, as he preferred to be called, was our saving grace for a while and Joey's symptoms began to improve. His tremors lessened, and things started to look up for a while. However, the treatment eventually showed diminishing returns.

L-DOPA helped us make up for the dopamine deficiency caused by the death of other dopaminergic neurons but his work could not keep up with the neuron deaths. The dopamine deficiency worsened and Joey's tremors came back with a vengeance. At this point in time, about five years ago, my neuron colleague who first informed of the incident in the olfactory bulb died. In the last five years, Joey has continued with the medication, but his short symptom relief and tremors have kept him from leading a comfortable, normal life. Two days ago, his physician informed him that he was a candidate for Deep Brain Stimulation, a surgical procedure that sends electrical signals to targeted areas of the brain.

"Won't that hurt my healthy brain tissue?", Joey asked, fearful of the implications of brain surgery.

"No", explained the doctor. "DBS uses a surgically implanted, battery-operated medical device called a neurostimulator, kind of like a heart pacemaker, to deliver electrical stimulation to targeted areas in the brain that control movement, blocking the abnormal nerve signals that cause your tremor and PD symptoms." This information came as a beacon of hope after L-DOPA could no longer help us and we waited to learn Joey's decision.

Joey knew he wanted relief from his symptoms and after careful consideration, he decided to undergo the procedure. The other dopaminergic neurons and I are now nervously awaiting the surgery and the results it will bring. I am afraid of not living to experience how Joey will feel after the surgery but hope he can finally live the semblance of a normal life and enjoy his remaining years. Therefore, I will continue my work as I always have, for however long I have left, with the support of the rest of my colleagues to manage his motor movement with the dopamine we still have available.

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